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(12) **UK Patent Application** (19) **GB** (11) **2 206 338** (13) **A**  
 (43) Application published 5 Jan 1989

(21) Application No 8810322

(22) Date of filing 29 Apr 1988

(30) Priority data

(31) 62/161367

(32) 30 Jun 1987

(33) JP

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(51) INT CL<sup>4</sup>

C01B 25/32

(52) Domestic classification (Edition J):

C1A D37 G47 G47D37 PB5

U1S 1028 C1A

(56) Documents cited

GB A 2063841

GB A 2010792

US 3679360

(58) Field of search

C1A

Selected US specifications from IPC sub-class

C01B

(54) Fine filler for dental purposes

(57) A fine filler for dental purposes comprises hydroxy-apatite or tetracalcium phosphate into which there is preferably incorporated an adjuvant such as a calcification-promoting protein. The fine filler may be presented as a powder, a granulate, a solution (suspension) or paste for rubbing on the surface of teeth.

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TITLE

FINE FILLER FOR DENTAL PURPOSES

BACKGROUND OF THE INVENTION

## Field of the invention

The present invention relates to a dental fine filler for protecting or restoring pits and fissures or minute decalcified surface lesions in enamel. The filler for rubbing onto the teeth, may be in the form of a powder, granules, solution (suspension) or paste.

## Description of the Prior Art

When plaque deposits on the surface of enamel, acids produced therein by microorganisms gradually etch the enamel and produce minute lesions therein. (This process is hereinafter referred to as decalcification. It is recognised that decalcified lesions are recalcified and restored by saliva). Once the enamel is decalcified, plaque is soon redeposited on the decalcified lesions, even though it is removed by brushing, so that the enamel is subjected to repeated decalcification due to acids. Thus, decalcification advances through repetitive occurrence of decalcification, removal of the plaque, redeposition of the plaque and decalcification, ending in visually detectable caries. In conventional dental treatment, the hard tissue of a visually detectable carious tooth including its periphery is resected, and various plastics, cements or metals are filled in the resected site as a replacement of the lesion. However, this method requires a high degree of technical skill. In addition, if filling is incomplete, the carious process again advances from the periphery of the filling material. In recent years, a sealant method has been developed in which the pits and fissures that are most susceptible to caries or decalcified lesions caused by the incipient decalcification are occluded with a sealant

that is a polyacrylate, polyurethane or other polymer to isolate them from the oral environment, thereby preventing caries from occurring. According to the sealant method, the pits and fissures or decalcified lesions, which may have been treated with acids depending upon the sealant agents used, are occluded therewith to prevent plaque from occurring and acting on the site, thereby preventing caries. In this method, however, insufficient or excessive acid treatment or deposition of saliva on the acid-treated surface may cause a decline in the bonding force of the sealants with respect to pits and fissures or decalcified lesions. The sealants, if occluded in too large an amount, may also break due to mastication and biting. Thus, with the sealant method, there is the possibility that the sealants may dislodge depending upon their quality and the technical skill of the operator, and the effectiveness of the method varies with the clinical skill of the operator. With the sealant method, difficulty is encountered in covering minute decalcified lesions with the sealant agents and in the recalcification of the covered decalcified lesions since they do not come into contact with saliva. In efforts to enhance resistance to caries by the reinforcement or protection of dentin, fluorine ions are applied to the surface of teeth or added to drinking water and foods. However, a special technique is required for the manipulation of fluorine compounds. As a method of depositing an enamel composition on the surface of teeth, Japanese Patent Application Laid-Open (KOKAI) No. 47-1567 proposes to form brassid on the surface of teeth using as the medium a gelatiniform substance prepared in such a manner that its toxicity and final pH do not harm the mouth, and to convert brassid to hydroxy-apatite. However, this method not only requires an extended period of time for the conversion of brassid to hydroxy-apatite, but also requires use of the gelatiniform substance so as to help

bond brassid to the surface of teeth.

Application of fluorine exists as a procedure for reinforcing the surface of teeth, and the sealant method or the method disclosed in Japanese Patent Application Laid-Open (KOKAI) No. 47-1567 is available as a procedure for protecting the pits and fissures and restoring decalcified lesions. However, these methods require special clinical skill and involve the difficulties mentioned above.

#### SUMMARY OF THE INVENTION

An object of the present invention is to provide a dental fine filler which can easily be applied in a short period of time with no need for any special clinical skill for safe protection and restoration of pits and fissures and decalcified lesions.

In one aspect, the invention comprises a fine filler for dental purposes comprising a powder, a granulate, a solution, a suspension or a paste containing hydroxy-apatite or tetracalcium phosphate. The fine filler may also if desired contain an adjuvant such as a fluoride, calcium phosphate or a calcification-promoting protein.

In another aspect, the invention comprises a fine filler for dental purposes, comprising a calcification-promoting protein incorporated in hydroxy-apatite or tetracalcium phosphate.

To evaluate the benefits of the fine filler of the invention, suspensions of finely divided hydroxy-apatite containing radioactive calcium and finely divided brassid were prepared and added to an artificial tooth prepared by sintering hydroxy-apatite for the immersion thereof. The upper face of the artificial tooth was rotatively abraded

through a rubber membrane. After elapse of a certain time, the artificial tooth was removed and, soon thereafter, a large mount of distilled water was added dropwise thereto for washing, followed by the addition of a PSC cocktail. Radioactivity of the artificial tooth was measured with a liquid scintillation counter, whereby the amounts of hydroxy-apatite and brassid bonded to the artificial tooth were determined. As a result, it was found that the bonded amounts depended upon the pH of the suspensions, but the amount of hydroxy-apatite bonded was much larger than the amount of brassid bonded in any pH range. It was also confirmed by nominal experimentation that tetracalcium phosphate  $[\text{Ca}_4(\text{PO}_4)_2\text{O}]$  obtained by sintering an equimolar mixture of tricalcium phosphate and calcium oxide at  $1500^\circ\text{C}$  bonded easily to a tooth, as was the case with hydroxy-apatite, and the tetracalcium phosphate bonded changed to hydroxy-apatite immediately upon contact with saliva to promote the recalcification of the tooth. The fact that these substances promote the recalcification of teeth and protect the teeth from decay was supported by the following experimentation. An extracted 3rd molar subjected to artificial caries was immersed under agitation in a hydroxy-apatite or tetracalcium phosphate paste at  $37^\circ\text{C}$  for 5 hours, and the surface enamel layer of the tooth was thereafter observed under a polarization microscope. As a result, decalcified lesions were found over a wide range of a control group, whereas a hydroxy-apatite or tetracalcium phosphate-treated group was recalcified on the surface layer, with the decalcified lesions being thinner than those of the control group. These indicate that hydroxy-apatite or tetracalcium phosphate is efficiency bonded to the surfaces of teeth to cover or cure the decalcified lesions and promote the calcification of enamel by contact with saliva. Thus, the present invention permits the protection of pits and

fissures and the restoration of decalcified lesions by making use of the properties of hydroxy-apatite or tetracalcium phosphate bonding selectively to the surface decalcified lesions of teeth.

It is desired that the hydroxy-apatite or tetracalcium phosphate to be used be as finely divided as possible. In general, they are finely divided to about 0.02 to 10 microns for use. The finely divided hydroxy-apatite or tetracalcium phosphate is preferably formulated to about a 5 to 95% solution (suspension) or paste with or without water or a coating agent. These materials are rubbed on a tooth, from which the plaque has been removed, with a fingertip, brush, stick, cloth or the like for at least 1 min, preferably 3 min. In the course of this operation, the hydroxy-apatite or tetracalcium phosphate is further finely divided and bonded to the pits and fissures or minute decalcified lesions of the enamel. Since the hydroxy-apatite or tetracalcium phosphate is the highest nutritive calcium substance, the patient may swallow extra calcium salts remaining in the mouth. Preferably, washing of the mouth with water should be carried out lightly and limited to about one time. The recalcification of the hydroxy-apatite or tetracalcium phosphate bonded to the tooth surface is promoted due to the presence of saliva.

It is preferred to use powders, granules, solutions (suspensions) or pastes of hydroxy-apatite or tetracalcium phosphate which are prepared by mixing with a suitable amount of an adjuvant selected from a phosphate such as tricalcium phosphate and monohydrogen calcium phosphate; a fluoride such as sodium fluoride, sodium monofluorophosphate, apatite fluoride and stannous fluoride; a calcification-promoting protein such as phosvitin, casein and hestidine-reci protein (these

proteins have been found to act as catalysts and accelerators for the calcification of hydroxy-apatite); or a mixture thereof, since the adjuvant promotes the recalcification of the decalcified lesions and reinforces the covered layer. The amounts of these adjuvants to be added may be selected arbitrarily depending upon their types. In general, however, the phosphate should be used in amounts of about 1 to 60%, the fluoride in an amount of 1000 ppm at most and the calcification-promoting protein in an amount of about 1% at most, with respect to the hydroxy-apatite and/or tetracalcium phosphate. A coating agent may advantageously be incorporated into the paste, and may be vinyl acetate, glue, polyacrylic acid, gum arabic or the like.

Thus, the hydroxy-apatite or tetracalcium phosphate is bonded to the surface of teeth merely by rubbing thereon the hydroxy-apatite or tetracalcium phosphate-containing paste, and is recalcified by saliva. The presence of the adjuvants serves to enhance such recalcification and the strength of teeth. Dental care using the filler of the present invention can easily be carried out without recourse to acid treatments, moisture-proofing and polymerization treatments applied in the conventional sealant method, and without any special clinical skill. Further, the hydroxy-apatite, tetracalcium phosphate, adjuvants and coating agents have no adverse influence upon the living body. Still further, the hydroxy-apatite is a component the same as that found in teeth, while the tetracalcium phosphate is easily converted to hydroxy-apatite by saliva. Thus, since these substances do not constitute foreign matter with respect to teeth, unlike the prior art sealant agents, and since they bond firmly to the pits and fissures and decalcified lesions with no risk of being dislodged, completely restored teeth are produced.

In addition, plasticizers, solvents, diluents and so on may be added to a paste comprising hydroxy-apatite or tetracalcium phosphate, together with the calcification-promoting protein and a coating agent in such a manner that the resulting system has a viscosity suitable for covering the surface of teeth and providing a film of uniform thickness. The application of such a system to the surface of teeth is advantageous in that the surface of teeth can be reinforced and improved in appearance.

It is also possible to use the filler of the invention by rubbing it onto the tooth surface followed by the application of fluoride in conventional manner. It is also possible to rub the filler on the surface of teeth and thereafter cover and protect the site with a polymer. The polymers used to this end may be selected from polymers so far used as the sealants, such as Epoxylight 9070, Nuva-Seal, Epoxylight 9075, Enamelight, Delton, White Sealant, F + F Sealant, Fissureseal, Teethmata S, Prisma Shield, Helioseal, or polymers used with sustained release preparations for pharmaceuticals such as shellac, polyvinyl acetate, polyvinyl butyral, ethyl cellulose, cellulose acetate phthalate, polyvinyl alcohol phthalate, styreneacrylic acid copolymers, methyl-methacrylic acid copolymers, copolymers of vinyl pyridine or alkyl pyridine with other vinyl monomers, cellulose acetate diethylaminoacetate, polyvinyl acetate diethylaminoacetate, polyvinyl aminoacetal, polyvinyl alcohol derivatives, amino cellulose derivatives, dimethylaminoethyl methacrylate-methyl methacrylate copolymers and copolymers of vinyl pyridine or alkylvinyl pyridine with acrylic acid. These polymers may be applied to the site in the conventional manner. The hydroxy-apatite or tetracalcium phosphate and adjuvants rubbed in place by this coating are retained on the surface of the teeth over an extended



period of time without being dislodged, and are efficiently recalcified. The hydroxy-apatite or tetracalcium phosphate and calcification-promoting protein-containing paste may be added with, e.g., pharmaceutically active components such as an abrasive selected from calcium carbonate, calcium hydrogen phosphate, aluminium hydroxide, silicic anhydride and other abrasives; a humectant such as glycerin, sorbitol and propylene glycol; a foaming agent such as sodium lauryl sulfate and soap powders; a binder such as carboxymethylcellulose and carrageenan; a perfume; a sweetener, a preservative; and a halitosis remover and tooth detinter. To use this system in a manner similar to a dentifrice provides a usable procedure which makes it possible to remove plaque simultaneously with rubbing of the hydroxy-apatite or tetracalcium phosphate and calcification-promoting protein on to the surface of teeth.

Thus, there is provided a filler for remedying the decalcification that is the incipient state of caries, which filler makes use of the properties of the adjuvant-containing or free hydroxy-apatite, which is the same component as tooth, or tetracalcium phosphate bonding selectively and firmly to the pits and fissures or decalcified lesions. Use of the tooth-reinforcing and caries-preventing filler does not require any special technical skill and has considerable technical advantages over the conventional fluoride coating and sealant methods.

Other features and advantages of the present invention will be apparent from the following description.

#### DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention will now be described in detail with reference to a number of examples.

##### Example 1

Fifty (50) g of hydroxy-apatite finely divided to 10 microns or less to which 50 ml of water was added was treated in a chaser mill to obtain a paste. Shortly after the teeth were brushed with a dentifrice followed by rinsing, the paste was carefully rubbed on the surface of the teeth with a fingertip for 3 min. Afterwards, excess paste was removed from within the mouth by light rinsing. This procedure was carried out whenever teeth were brushed.

#### Example 2

Fifty (50) g of hydroxy-apatite finely divided to 10 microns or less to which 50 ml of an aqueous solution containing 500 ppm of sodium fluoride was added was treated in a chaser mill to obtain a paste. At the completion of ordinary brushing, teeth were brushed for 3 min with a toothbrush to which paste was applied. This was followed by light rinsing. This brushing was always carried out after ordinary brushing.

#### Example 3

Fifty (50) g of hydroxy-apatite finely divided to 10 microns or less to which 50 ml of water containing 0.01 mg of casein was added was treated in a chaser mill to obtain a paste. At the completion of ordinary brushing, the paste was carefully rubbed on the surface of the teeth with a fingertip for 3 min. This procedure was carried out whenever teeth were brushed.

#### Example 4

In a manner similar to that described in Example 3, the paste was rubbed on the surface of teeth and excess paste within the mouth was then washed away by rinsing. Following drying, a Nuva-Seal liquid was thinly applied to the surface of the teeth and was hardened by an ultraviolet lamp for sealing purposes.

In a manner similar to that described in Example 3, the paste was rubbed on the surface of teeth and excess paste within the mouth was then washed away by rinsing. Diamine silver fluoride was applied in the conventional manner.

#### Example 6

Four (4) g of hydroxy-apatite finely divided to 10 microns or less and 0.04 mg of casein were added to and mixed sufficiently with 100 ml of vinyl acetate to prepare a homogeneous dispersion. After ordinary brushing, the teeth were dried with warm air and then uniformly coated with the dispersion by means of a brush. Drying gave a glossy, white and fine coating on the surface of the teeth.

#### Example 7

Fifty (50) g of tetracalcium phosphate finely divided to 10 microns or less to which 50 ml of water was added was treated in a chaser mill to obtain a paste. Shortly after teeth were brushed with a dentifrice followed by thorough rinsing, the paste was carefully rubbed on the surface of the teeth with a fingertip for 3 min. Afterwards, excess paste was removed from within the mouth by light rinsing. This procedure was carried out whenever teeth were brushed.

#### Example 8

Fifty (50) g of tetracalcium phosphate finely divided to 10 microns or less, to which 50 ml of an aqueous solution containing 50 ppm of sodium fluoride had been added, was treated in a chaser mill to obtain a paste. At the completion of ordinary brushing, teeth were brushed for 3 min with a toothbrush to which the paste was applied. This was followed by light rinsing. This brushing was always carried out after ordinary brushing.

#### Example 9

Fifty (50) g of tetracalcium phosphate finely divided to 10 microns or less to which 50 ml of water containing 0.01 mg of casein was added was treated in a chaser mill to obtain a paste. At the completion of ordinary brushing, the paste was carefully rubbed on the surface of the teeth with a fingertip for 3 min. This procedure was carried out whenever teeth were brushed.

#### Example 10

In a manner similar to that described in Example 3, the paste was rubbed on the surface of teeth and excess paste within the mouth was then washed away by rinsing. Following drying, a Nuva-Seal liquid was thinly applied to the surface of the teeth and was hardened by an ultraviolet lamp for sealing purposes.

#### Example 11

Four (4) g of tetracalcium phosphate finely divided to 10 microns or less and 0.04 mg of casein were added to and mixed sufficiently with 100 ml of vinyl acetate to prepare a homogeneous dispersion. After ordinary brushing, the teeth were dried with warm air and then uniformly coated with the dispersion by means of a brush. Drying gave a glossy, white and fine coating on the surface of the teeth.

#### Reference Examples

In order to measure the amount of hydroxy-apatite bonded to the surface of a tooth, the following in vitro tests were conducted:

(A) Synthesis of hydroxy-apatite and brassid

One hundred (100) ml of a 0.1 M  $\text{CaCl}_2$  solution (containing  $^{45}\text{CaCl}_2$  manufactured by Aeroham) was slowly added dropwise, under agitation, to 100 to 200 ml of 0.1M  $\text{Na}_2\text{HPO}_4$  solutions to synthesize hydroxy-apatite in the conventional manner. On the other hand, a 0.1M  $^{45}\text{CaCl}_2$

solution was similarly added dropwise to 100 to 200 ml of 0.01  $\text{NaH}_2\text{PO}_4$  solutions to prepare brassid. After preparation, the hydroxy-apatite and brassid were preserved in the corresponding 0.1 M  $\text{Na}_2\text{HPO}_4$  and 0.1 M  $\text{NaH}_2\text{PO}_4$  solutions. For use, they were resuspended in 0.1 M phosphoric acid buffers of the corresponding pH.

(B) Preparation of artificial tooth

The hydroxy-apatite was moulded into a disc which was 1 cm in diameter and 3 mm in thickness, and the disc was sintered to form a hydroxy-apatite tablet, the surface of which was evenly abraded with No. 600 sand paper. Afterwards, the tablet was brushed to carefully remove powders, while distilled water flowed thereover, thereby making an artificial tooth.

(C) An acrylic tank which was 12 cm in length, 4 cm in width and 10 mm in depth was provided in its bottom with five blind holes for the fixation of hydroxy-apatite tablets, each of which was 1 cm in diameter and 2 mm in depth. Five hydroxy-apatite tablets were fixed in the blind holes and 5 ml of a hydroxy-apatite or brassid suspension was added to immerse the tablets. The upper surface of the tablets was abraded at 1 rpm. Upon elapse of a certain time, the tablets were removed and, soon thereafter, washed by dropwise addition of a large amount of distilled water. Two (2) ml of a PSC cocktail was added to the tablets to measure the radioactivity of the tablets with a liquid scintillation counter.

(D) Results

As the results of tests performed at pH 9.0 and 5.0 that were the stable pH of hydroxy-apatite and brassid, respectively, the amount of hydroxy-apatite bonded to the tablets was 5 micrograms after 5 min. Thereafter, this

increased gradually and reached 164 micrograms after 40 min, as calculated from  $5.4 \times 10^5$  CPM/mg and  $8.9 \times 10^5$  CPM/mg that were the specific radioactivities of the hydroxy-apatite and brassid used, respectively. This bonded amount was much larger than that of brassid by a factor of 20 after 5 min and 109 after 40 min.

From the results of tests performed at pH 5.5, 6.8, 7.4 and 8.5, where rubbing was carried out at the same pH, it was also found that the bonding force of hydroxy-apatite to the tablets was markedly increased.

These results are tabulated below

pH Condition	A/B	
	After 10 min	After 60 min
A: pH 9, B: pH 5	32.8	201.7
A, B pH 8.5	2.0	5.4
" pH 7.4	6.6	5.4
" pH 6.8	2.3	6.4
" pH 5.5	11.2	8.4

A: hydroxy-apatite; B: brassid

Figures represent the amounts in weight ratio of hydroxy-apatite and tetracalcium phosphate bonded to the tablets.

These results reveal that hydroxy-apatite is selectively bonded to the surface of teeth.

Thus, to use the filler of the present invention, a fine filler containing hydroxy-apatite that is a biomaterial firmly bonding to the pits and fissures or minute decalcified lesions in the surfaces of teeth or tetracalcium phosphate with or without adjuvants is rubbed on the surface of teeth, optionally followed by covering the thus rubbed site with a polymer, to cover the pits and

fissures or decalcified lesions with the fine filler, so that spontaneous healing power is augmented under the action of saliva or the adjuvants for the restoration of the decalcified lesions. This method exhibits excellent effects merely by rubbing the fine filler on the surface of teeth. Since hydroxy-apatite or tetracalcium phosphate is the most ideal calcium substance, it is harmless if swallowed and the filler can be used without fear of harmful effects. No special clinical skill is required to carry out this method. Accordingly, the use of the filler of the invention is advantageous in that it can easily be carried out by the patient himself.

The present method in which caries is suppressed in its incipient stage by making use of, and augmenting, spontaneous healing power obtained through recalcification by saliva is the most effective means for preventing caries that is not found in the prior art. The filler of the present invention is also useful in the treatment of paresthesia and pyrrhoea alveolaris.

CLAIMS

1. A fine filler for dental purposes comprising a powder, a granulate, a solution, a suspension or a paste containing hydroxy-apatite or tetracalcium phosphate.
2. A fine filler according to claim 1, in which the powder, granulate, solution, suspension or paste also contains an adjuvant.
3. A fine filler according to claim 2, wherein the adjuvant is a fluoride or calcium phosphate.
4. A fine filler according to claim 2, wherein the adjuvant is a calcification-promoting protein.
5. A fine filler according to any preceding claim, wherein the powder, granulate, solution, suspension or paste also contains a coating agent.
6. A fine filler for dental purposes, comprising a calcification-promoting protein incorporated in hydroxy-apatite or tetracalcium phosphate.
7. A fine filler according to claim 6, further comprising a coating agent incorporated in the hydroxy-apatite or tetracalcium phosphate.
8. A fine filler according to claim 6 or claim 7, having a particle size of from 0.02 to 10 microns.
9. A fine filler according to any of claims 6 to 8, in the form of a solution, suspension or paste comprising from 9 to 95% of the hydroxy-apatite or tetracalcium phosphate.
10. A fine filler according to any of claims 6 to 9,



further incorporating an adjuvant comprising a fluoride or calcium phosphate.

11. A fine filler for dental purposes, substantially as disclosed in any of the Examples herein.